Dementia

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Objectives

Provide an overview of dementia prevalence and impact

Review types of cognitive impairment/dementias

Discuss various pharmalogical treatments of different types of dementias

Provide discussion surrounding reversible causes of dementia

Provide tools for screening for cognitive impairment and interpretation of these tools

Dementia Prevalence

Alzheimer's Disease (AD) accounts for 60-80% of all dementia cases

5.7 million Americans are diagnosed with AD (majority of 65+)

5th leading cause of death

Survival: 4-8 years (up to 20 years)

2050 → 19 million impacted

Health Care Cost Implications

Caregiving responsibilities

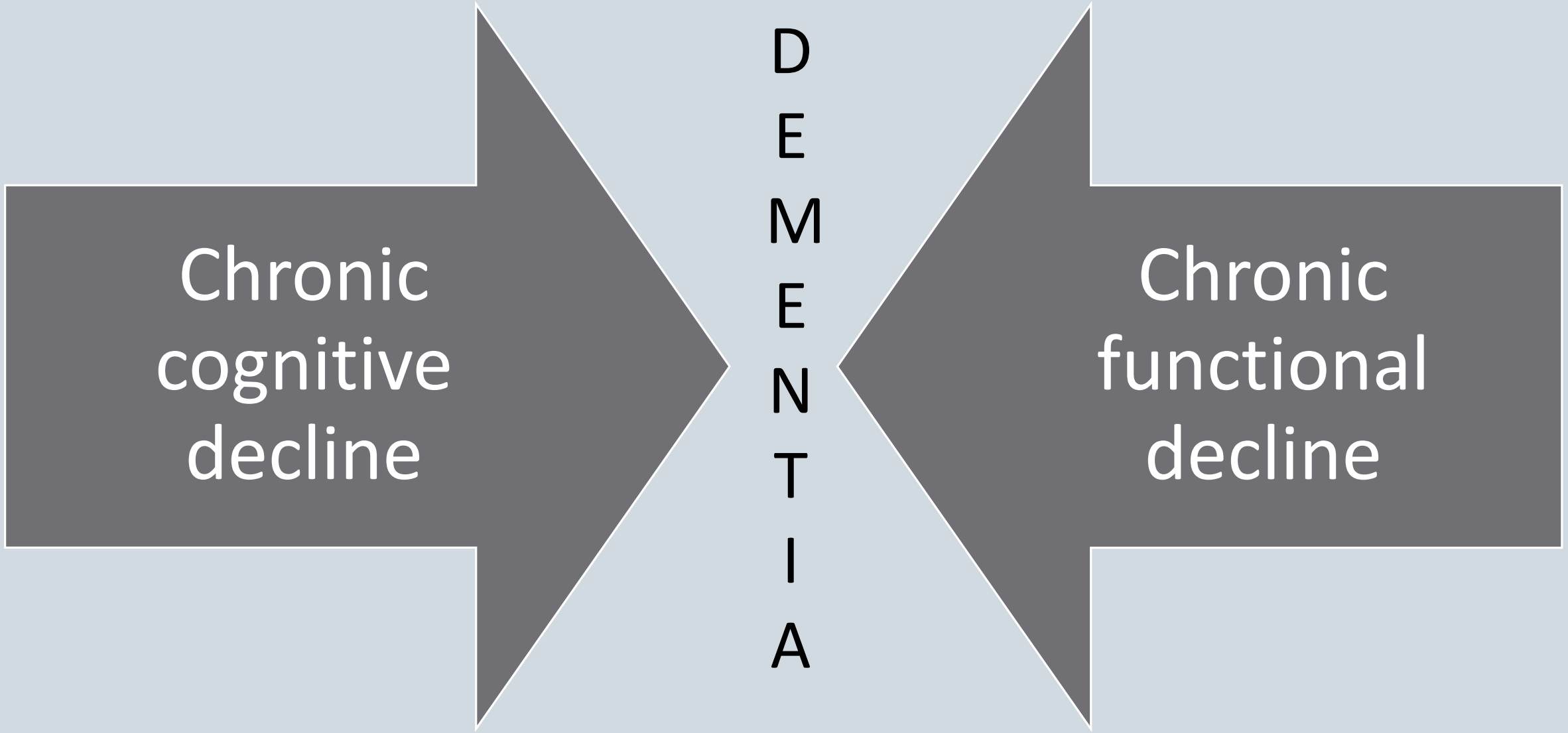
2010 – paid & unpaid caregiving expenses: $159-215 billion

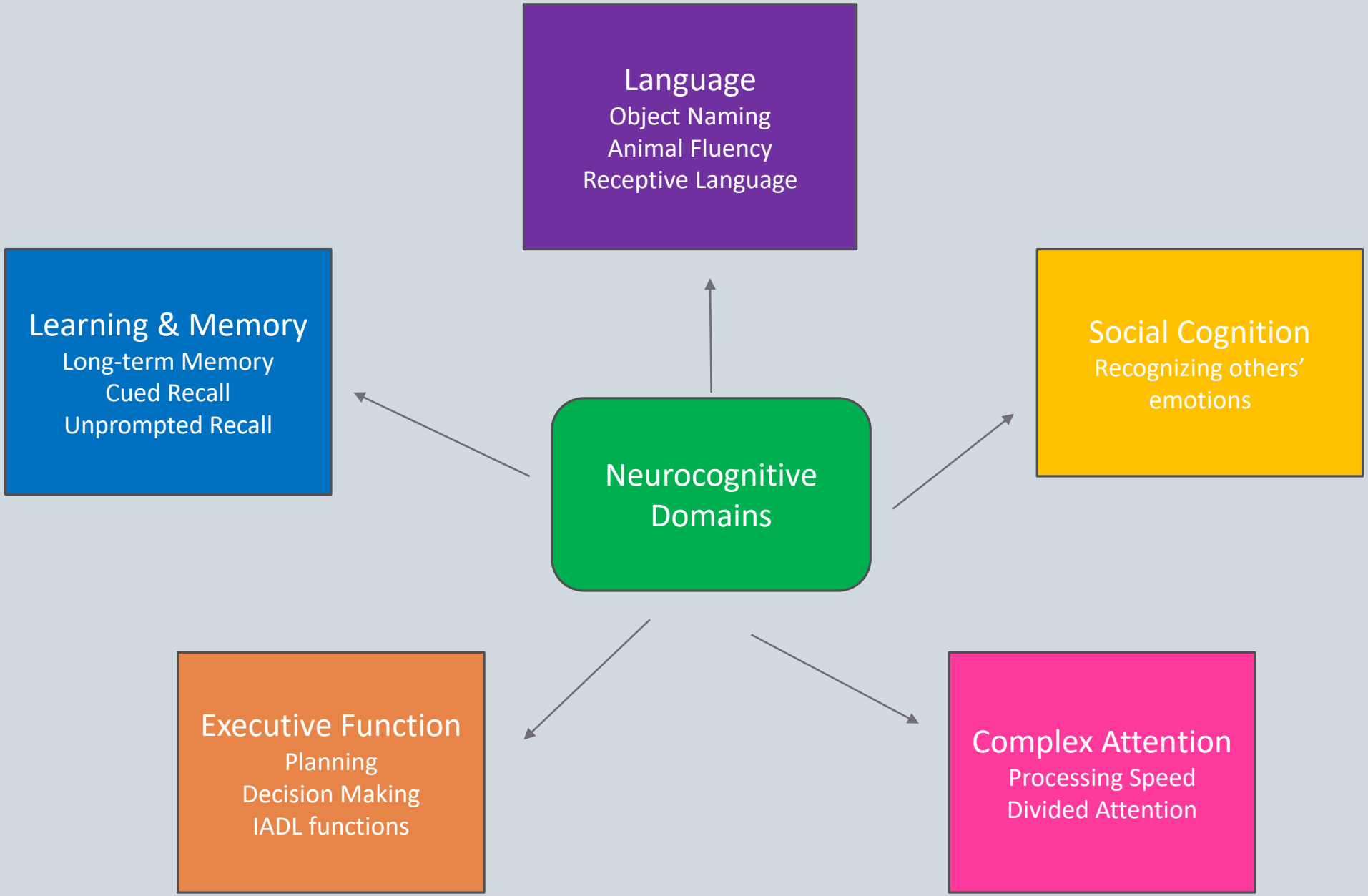
Costs: Direct Medical Expenditures

Long term care

Home & Community Based Supports

Unpaid Family Caregivers (e.g. lost wages)


Chronic cognitive decline
DEMENTIA
Chronic functional decline


Language
Object Naming
Animal Fluency
Receptive Language
Learning & Memory
Long-term Memory
Cued Recall
Unprompted Recall
Neurocognitive Domains
Social Cognition
Recognizing others' emotions
Executive Function
Planning
Decision Making
IADL functions
Complex Attention
Processing Speed
Divided Attention

Cognitive Screens

- Mini-Cog
- MMSE*
- SLUMs
- MOCA*
- Blind MOCA

*Now propriety tests

MiniCog Test

1. 3 Item Repeat

   Banana Sunrise Chair

   Village Kitchen Baby

2. Clock Draw Task

3. 3 Item Recall

https://mini-cog.com/

Mini Cog

Normal Clock

Abnormal Clock

(abnormal hands)

Abnormal Clock

(missing number)

higher. When greater sensitivity is desired, a cut point of <4 is recommended as it may indicate a need for further evaluation of cognitive status.

VAMC
SLUMS Examination

Questions about this assessment tool? E-mail aging@slu.edu

Name _____ Age _____

Is the patient alert? _____ Level of education _____

__/1 (1) 1. What day of the week is it?

__/1 (1) 2. What is the year?

__/1 (1) 3. What state are we in?

4. Please remember these five objects. I will ask you what they are later.
Apple Pen Tie House Car

5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20.
(1) How much did you spend?
__/3 (2) How much do you have left?

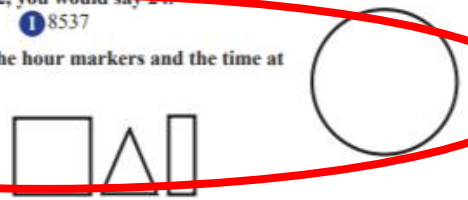
6. Please name as many animals as you can in one minute.
__/3 (0) 0-4 animals (1) 5-9 animals (2) 10-14 animals (3) 15+ animals

__/5 7. What were the five objects I asked you to remember? 1 point for each one correct.

8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.
__/2 (0) 87 (1) 648 (1) 8537

9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
(2) Hour markers okay
__/4 (2) Time correct

(1) 10. Please place an X in the triangle.



__/2 (1) Which of the above figures is largest?

11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.

Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.

__/8 (2) What was the female's name? (2) What work did she do?
(2) When did she go back to work? (2) What state did she live in?

_____ TOTAL SCORE

SCORING

High School Education		Less than High School Education
27-30	Normal	25-30
21-26	Mild Neurocognitive Disorder	20-24
1-20	Dementia	1-19

CLINICIAN'S SIGNATURE _____ DATE _____ TIME _____

SH Tariq, N Tumosa, JT Chibnall, HM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for detecting mild cognitive impairment and dementia is more sensitive than the Mini-Mental Status Examination (MMSE): A pilot study. *Am J Geriatr Psych* 14:900-10, 2006.

https://www.slu.edu/medicine/internal-medicine/geriatric-medicine/aging-successfully/pdfs/slums_form.pdf

Differential Diagnosis

Untreated Depression

Untreated Insomnia

Untreated Pain

Delirium

- Infection
- Setting (e.g. inpatient vs outpatient)

Lab Tests – Differential Diagnosis

Labs	Rational
Vitamin B12	Neurological complications if <400pg/mL
TSH	Rule out hypothyroidism or hyperthyroidism
CBC	Anemia differential & Infection
BMP	Renal and Hepatic dysfunction
HIV	If risk factors exists
Syphilis	If risk factors exists

Medication Causing CNS Depressant Effects
Benzodiazepines
Sedatives/Hypnotics
Anticholinergics
Corticosteroids
Opioids

Anticholinergic Cognitive Burden Scale

Drugs with ACB Score of 1

Generic Name	Brand Name
Alimemazine	Theralen™
Alverine	Spasmonal™
Alprazolam	Xanax™
Aripiprazole	Abilify™
Asenapine	Saphris™
Atenolol	Tenormin™
Bupropion	Wellbutrin™, Zyban™
Captopril	Capoten™
Cetirizine	Zyrtec™
Chlorthalidone	Diuril™, Hygroton™
Cimetidine	Tagamet™
Clidinium	Librax™
Clorazepate	Tranxene™
Codeine	Contin™
Colchicine	Colcrys™
Desloratadine	Clarinex™
Diazepam	Valium™
Digoxin	Lanoxin™
Dipyridamole	Persantine™
Disopyramide	Norpace™
Fentanyl	Duragesic™, Actiq™
Furosemide	Lasix™
Fluvoxamine	Luvox™
Haloperidol	Haldol™
Hydralazine	Apresoline™
Hydrocortisone	Cortef™, Cortaid™
Iloperidone	Fanapt™
Isosorbide	Isordil™, Ismo™
Levocetirizine	Xyzal™
Loperamide	Immodium™, others
Loratadine	Claritin™
Metoprolol	Lopressor™, Toprol™
Morphine	MS Contin™, Avinza™
Nifedipine	Procardia™, Adalat™
Paliperidone	Invega™
Prednisone	Deltasone™, Sterapred™
Quinidine	Quinaglute™
Ranitidine	Zantac™
Risperidone	Risperdal™
Theophylline	Theodur™, Uniphyl™
Trazodone	Desyrel™
Triamterene	Dyrenium™
Venlafaxine	Effexor™
Warfarin	Coumadin™

Drugs with ACB Score of 2

Generic Name	Brand Name
Amantadine	Symmetrel™
Belladonna	Multiple
Carbamazepine	Tegretol™
Cyclobenzaprine	Flexeril™
Cyproheptadine	Periactin™
Loxapine	Loxitane™
Meperidine	Demerol™
Methotrimeprazine	Levoprome™
Molindone	Moban™
Nefopam	Nefogesic™
Oxcarbazepine	Trileptal™
Pimozide	Orap™

Categorical Scoring:

- Possible anticholinergics include those listed with a score of 1; Definite anticholinergics include those listed with a score of 2 or 3

Numerical Scoring:

- Add the score contributed to each selected medication in each scoring category
- Add the number of possible or definite Anticholinergic medications

Notes:

- Each definite anticholinergic may increase the risk of cognitive impairment by 46% over 6 years. [3]
- For each on point increase in the ACB total score, a decline in MMSE score of 0.33 points over 2 years has been suggested. [4]
- Additionally, each one point increase in the ACB total score has been correlated with a 26% increase in the risk of death. [4]

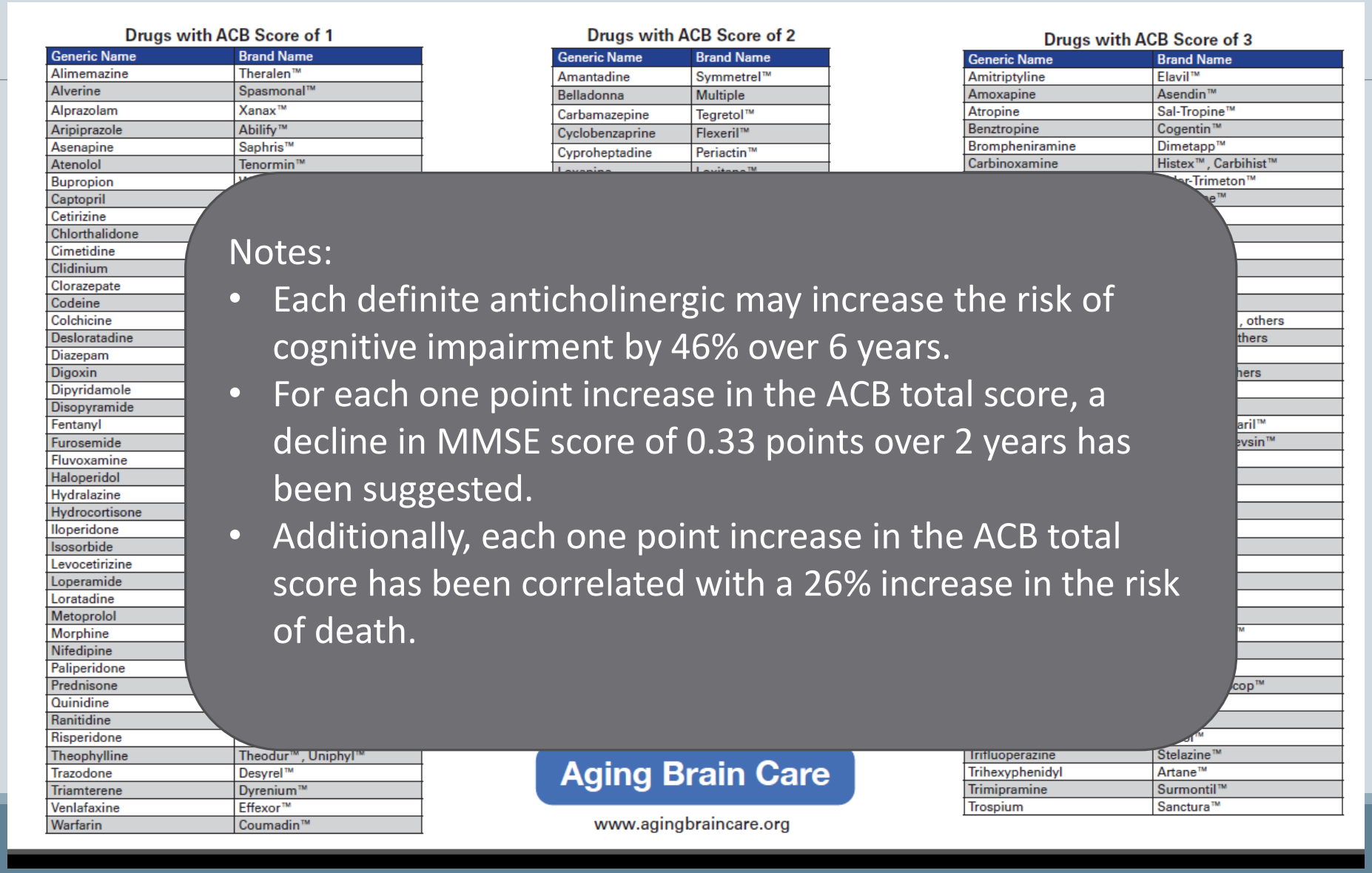
Aging Brain Care

www.agingbraincare.org

Drugs with ACB Score of 3

Generic Name	Brand Name
Amitriptyline	Elavil™
Amoxapine	Asendin™
Atropine	Sal-Tropine™
Benztropine	Cogentin™
Brompheniramine	Dimetapp™
Carbinoxamine	Histex™, Carbihist™
Chlorpheniramine	Chlor-Trimeton™
Chlorpromazine	Thorazine™
Clemastine	Tavist™
Clomipramine	Anafranil™
Clozapine	Clozaril™
Darifenacin	Enablex™
Desipramine	Norpramin™
Dicyclomine	Bentyl™
Dimenhydrinate	Dramamine™, others
Diphenhydramine	Benadryl™, others
Doxepin	Sinequan™
Doxylamine	Unisom™, others
Fesoterodine	Toviaz™
Flavoxate	Urispas™
Hydroxyzine	Atarax™, Vistaril™
Hyoscyamine	Anaspaz™, Levsin™
Imipramine	Tofranil™
Meclizine	Antivert™
Methocarbamol	Robaxin™
Nortriptyline	Pamelor™
Olanzapine	Zyprexa™
Orphenadrine	Norflex™
Oxybutynin	Ditropan™
Paroxetine	Paxil™
Perphenazine	Trilafon™
Promethazine	Phenergan™
Propantheline	Pro-Banthine™
Propiverine	Detrunorm™
Quetiapine	Seroquel™
Scopolamine	Transderm Scop™
Solifenacin	Vesicare™
Thioridazine	Mellaril™
Tolterodine	Detrol™
Trifluoperazine	Stelazine™
Trihexyphenidyl	Artane™
Trimipramine	Surmontil™
Trospium	Sanctura™

Anticholinergic Cognitive Burden Scale



Drugs with ACB Score of 1

Generic Name	Brand Name
Alimemazine	Theralen™
Alverine	Spasmonal™
Alprazolam	Xanax™
Aripiprazole	Abilify™
Asenapine	Saphris™
Atenolol	Tenormin™
Bupropion	
Captopril	
Cetirizine	
Chlorthalidone	
Cimetidine	
Clidinium	
Clorazepate	
Codeine	
Colchicine	
Desloratadine	
Diazepam	
Digoxin	
Dipyridamole	
Disopyramide	
Fentanyl	
Furosemide	
Fluvoxamine	
Haloperidol	
Hydralazine	
Hydrocortisone	
Iloperidone	
Isosorbide	
Levocetirizine	
Loperamide	
Loratadine	
Metoprolol	
Morphine	
Nifedipine	
Paliperidone	
Prednisone	
Quinidine	
Ranitidine	
Risperidone	
Theophylline	Theodur™, Uniphyl™
Trazodone	Desyrel™
Triamterene	Dyrenium™
Venlafaxine	Effexor™
Warfarin	Coumadin™

Drugs with ACB Score of 2

Generic Name	Brand Name
Amantadine	Symmetrel™
Belladonna	Multiple
Carbamazepine	Tegretol™
Cyclobenzaprine	Flexeril™
Cyproheptadine	Periactin™

Drugs with ACB Score of 3

Generic Name	Brand Name
Amitriptyline	Elavil™
Amoxapine	Asendin™
Atropine	Sal-Tropine™
Benztropine	Cogentin™
Brompheniramine	Dimetapp™
Carbinoxamine	Histex™, Carbihist™
Trifluoperazine	Stelazine™
Trihexyphenidyl	Artane™
Trimipramine	Surmontil™
Trospium	Sanctura™

Notes:

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Aging Brain Care

www.agingbraincare.org

DSM 5 Neurocognitive Disorder

Mild Neurocognitive Disorder

- Mild Cognitive Impairment (MCI)

Major Neurocognitive Disorder

- Dementia

Dementia Types

Alzheimer disease

Vascular dementia

Dementia with Lewy bodies

Mixed dementia

Other (eg, Parkinson disease dementia, Frontotemporal dementia, Huntington disease, Creutzfeldt–Jakob disease)

Potentially reversible causes of cognitive dysfunction (eg, normal pressure hydrocephalus, thyroid dysfunction, vitamin B12 deficiency, delirium, depression, Wernicke–Korsakoff syndrome)

Joseph T. DiPiro, Gary C. Yee, L. Michael Posey, Stuart T. Haines, Thomas D. Nolin, Vicki Ellingrod+
TABLE 71-1Common Types of Dementia

Cunningham EL, et al. Ulster Med J 2015;84(2):80

Dem

Alzheime

Vascular

Dementi

Mixed de

Other (eg n disease, Creutzfeldt

Potential essure hydroceph on, Wernicke–Korsakoff s

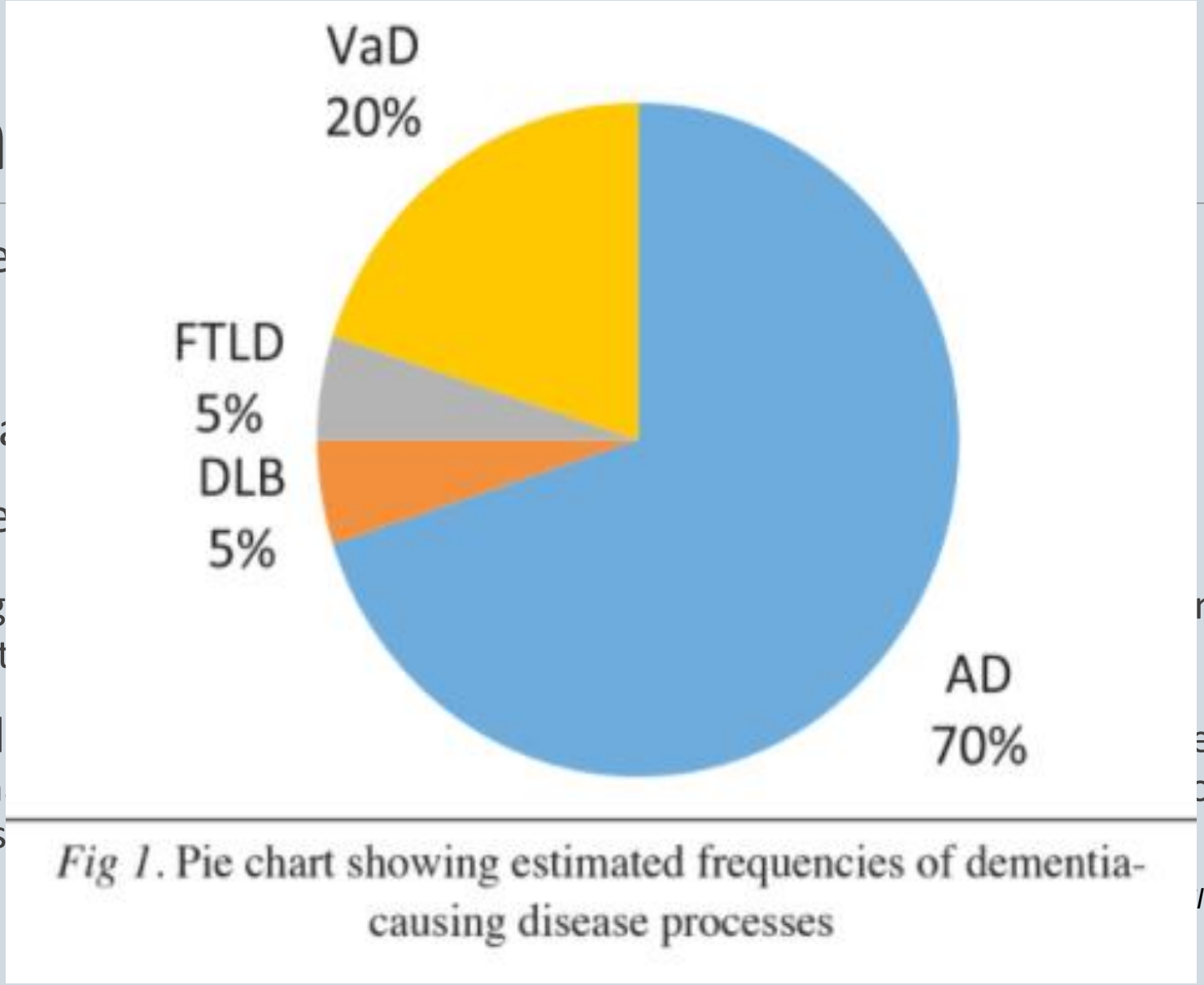
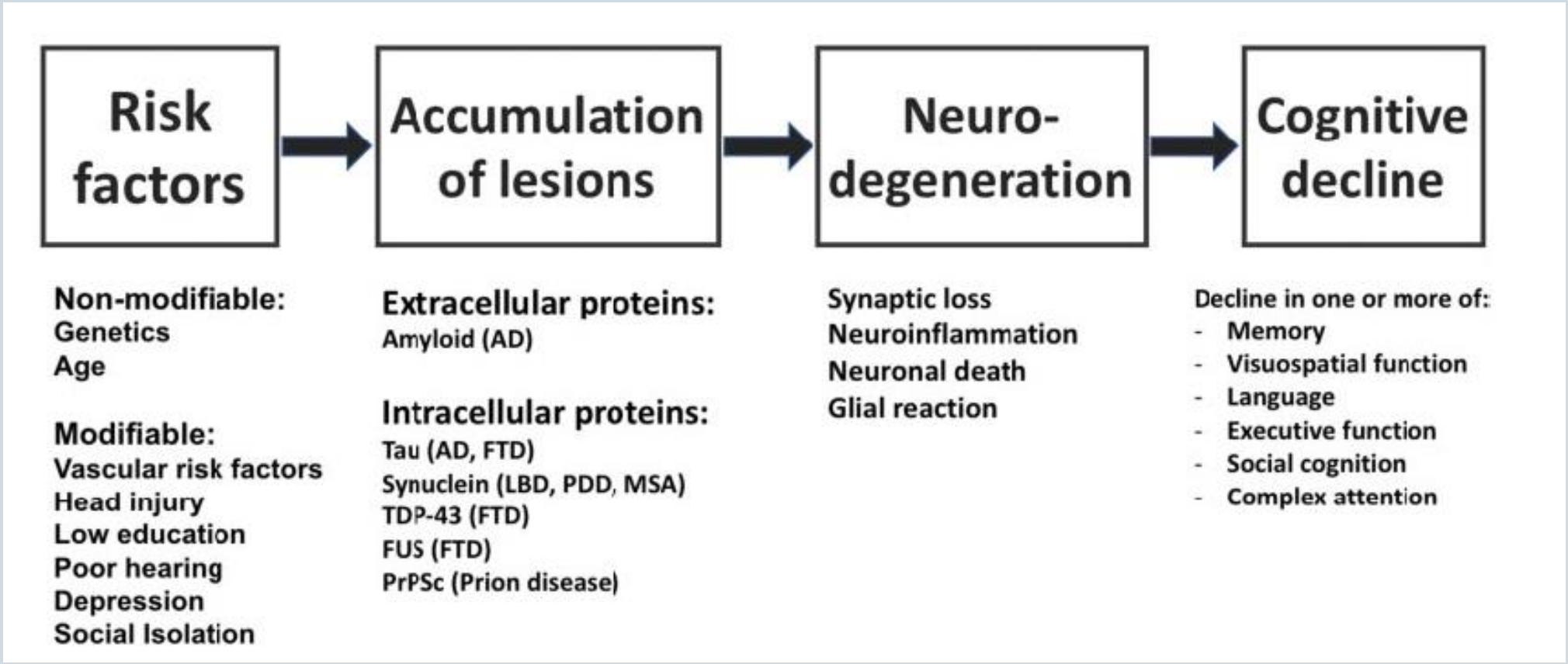


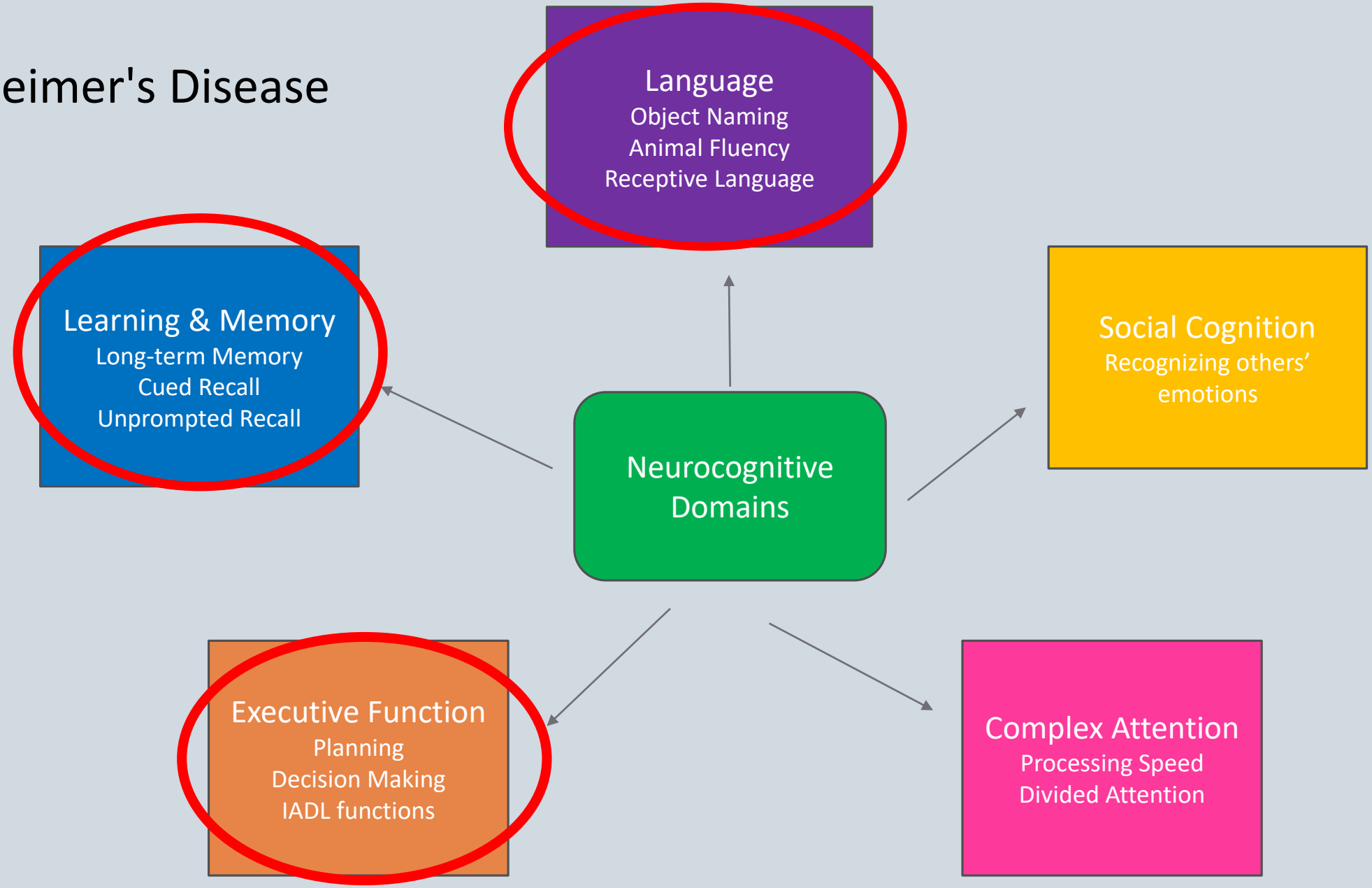
Fig 1. Pie chart showing estimated frequencies of dementia-causing disease processes

llingrod+

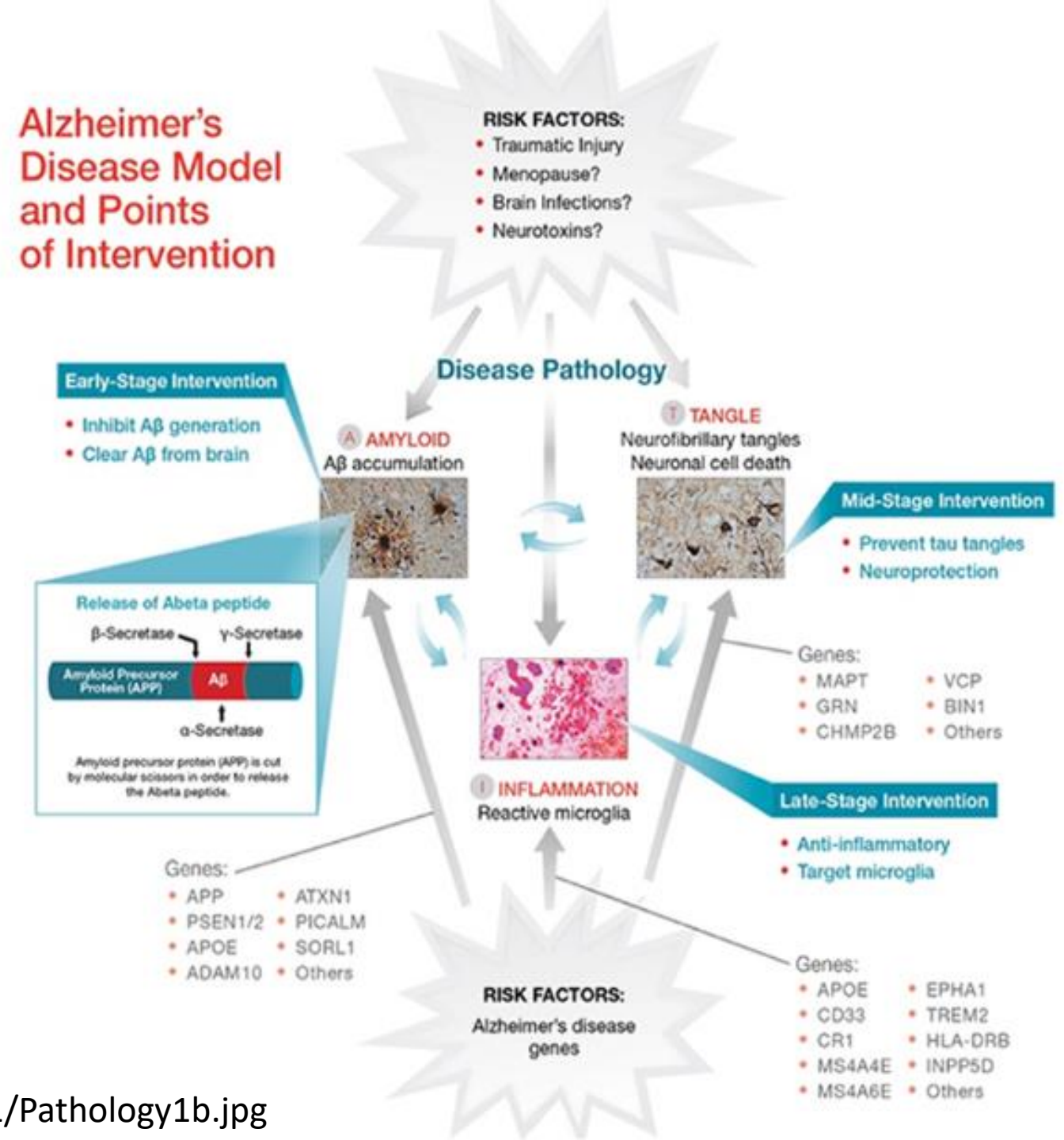
Etiology of Alzheimer's Disease



Alzheimer's Disease

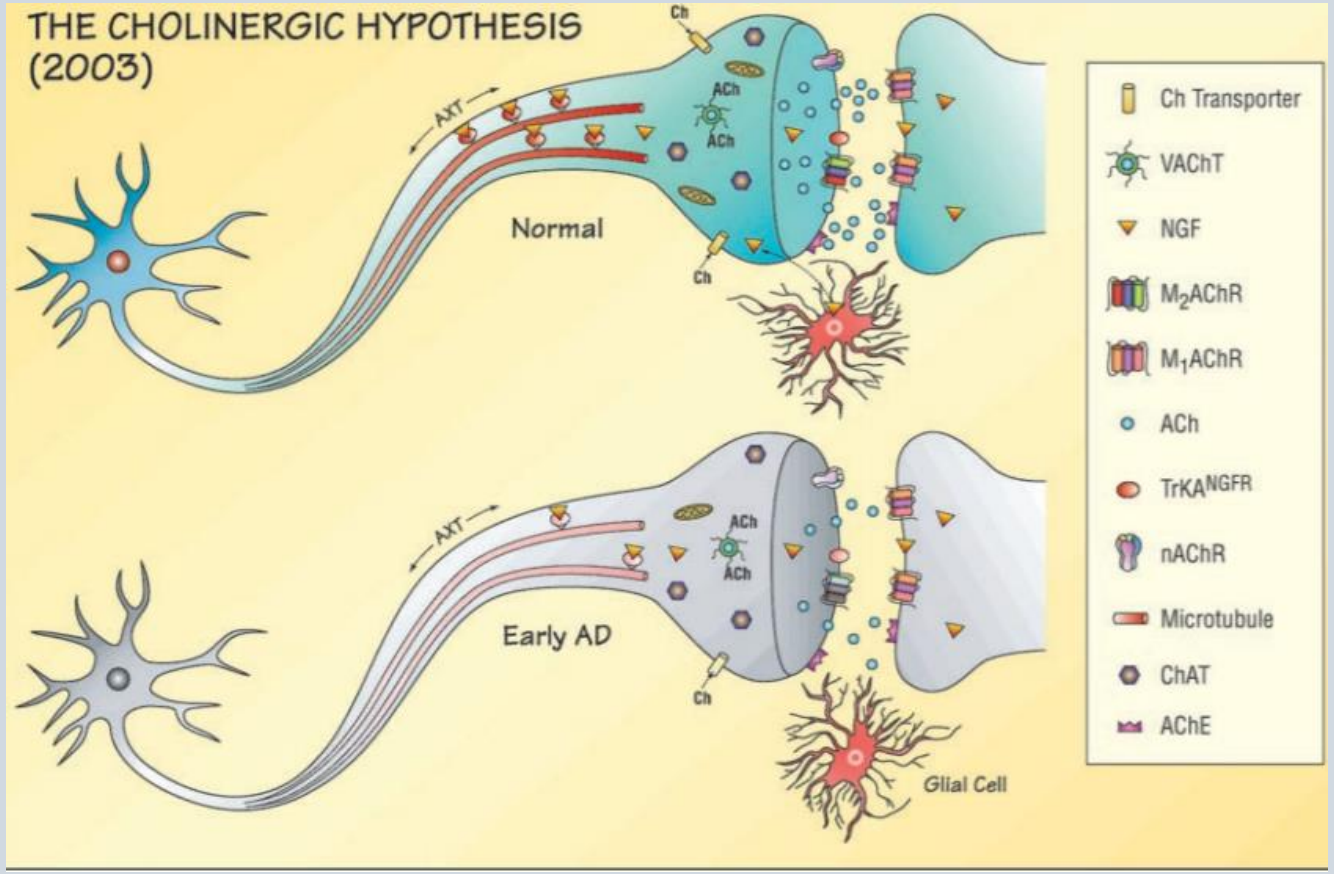


Pathophysiology



https://curealz.org/wp-content/uploads/2018/01/Pathology1b.jpg

Cholinergic Hypothesis



Terry JR AV and Buccafusco JJ. J Pharm and Exper Thera 2003;306(3):823

Clinical Presentation - AD

Symptoms

Cognitive

- Memory loss (poor recall and losing items)
- Aphasia (circumlocution and anomia)
- Apraxia
- Agnosia
- Disorientation (impaired perception of time and unable to recognize familiar people)
- Impaired executive function

Neuropsychiatric

- Depression, psychotic symptoms (hallucinations and delusions)
- Behavioral disturbances (physical and verbal aggression, motor hyperactivity, uncooperativeness, wandering, repetitive mannerisms and activities, and combativeness)

Functional

- Inability to care for self (dressing, bathing, toileting, and eating)

Diprio. Alzheimer's Disease

Disease Progression – Alzheimer's

Phases of AD	Symptoms Present
Preclinical Phase	Neuropathological changes present No or Subtle Symptoms
Mild Cognitive Impairment (MCI)	Memory Symptoms Present ADLs intact/ no functional deficits
Dementia	Functional Impairments (ADLs impacted)

Cognitive Function

https://www.x-zlab.com/radiation/radiation-exposure-alzheimers-disease-study/attachment/brain-shrinkage-dementia-alzheimers-qbi/

Treatment - AD

Mild to Moderate AD

- Donepezil (Aricept®)
- Galantamine (Reminyl®)
- Rivastigmine (Exelon®)

Moderate to Severe AD

- Donepezil (Aricept®)
- Rivastigmine Transdermal Patch (13.3mg dose)
- Memantine (Nemenda®)

Treatment - AD

Medication Name	Formulation	Dosing Schedule	Max Dose
Donepezil (Aricept®)	Tablets	2.5mg daily *titrate every 2-4 weeks as tolerated*	10mg daily
Galantamine (Reminyl®)	IR or ER tablets	8mg daily *Titrate 8mg every 4 weeks as tolerated*	24mg daily
Rivastigmine (Exelon®)	Capsules or Oral Soln Transdermal Patch	1.5mg BID *Titrate 3mg daily every 2 weeks as tolerated* 4.6mg/24 hours *Titrate up to 9.5mg/24 as tolerated after 4 weeks*	6mg BID 13.3mg/24 hours
Memantine (Namenda®)	Tablet – IR Tablet – XR Oral Solution (10mg/5mL)	5mg daily *Titrate up 5mg every 1-2 weeks as tolerated* 7mg daily *Titrate up by 7mg every 1-2 weeks as tolerated*	20mg daily 28mg daily

Treatment - AD

Side Effects:

Acetylcholinesterase inhibitors →

- GI Effects (N/V, diarrhea, upset stomach)
- Bradycardia
- Syncope
- Insomnia/Agitation
- Urinary Frequency

NMDA →

- Hypertension
- Hypotension
- Dizziness
- Aggressive Behavior
- Urinary Incontinence

Treatment - AD

Counseling Pearls:

Acetylcholinesterase Inhibitors

- Dose in the AM
- Take with food
- Baseline HRs needed

Both agents should counsel on perceived benefit of these agent to present appropriate expectations

Treatment - AD

Counseling P

Acetylcholi

- Dose in t
- Take with
- Baseline

Both agent ate expectatio

Discontinuation of AD Treatments:

- No tx response within 3 months
- Institutionalization patients with severe dementia treated ≥ 2 years
- Patient/family believe patient has stopped responding
- Progression of disease that goal of slowing progression is no longer reasonable

Treatment: Medical Foods - AD

Name	Formulation	Instructions	Indication
Caprylidene (Axona®)	Medium chained triglycerides *Powder*	Initial: 8-10g/day for 2 days, increase 8-10g/day every other days as tolerated Maintenance: 40g/day *taken after food*	Mild to Moderate AD
Cerefolin NAC®	Folic Acid Vitamin B12 N-acetylcysteine *Tablet*	1 caplet daily	Mild Cognitive Impairment
Vayacog®	Phosphatidylserine Docasahexaeonic Acid Eicosapentaenoic Acid *Tablet*	1 capsule daily	Early Memory Impairment

Lifestyle Modifications - AD

Omega 3 Supplements

Folic Acid

Vitamin B supplements

Vitamin E

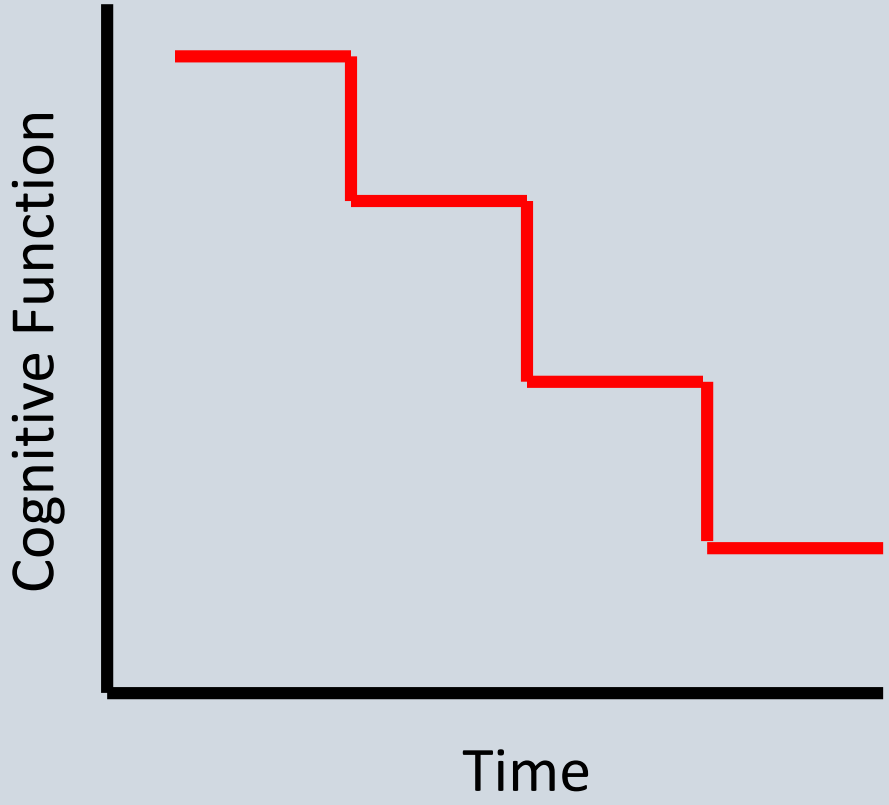
Physical Activity

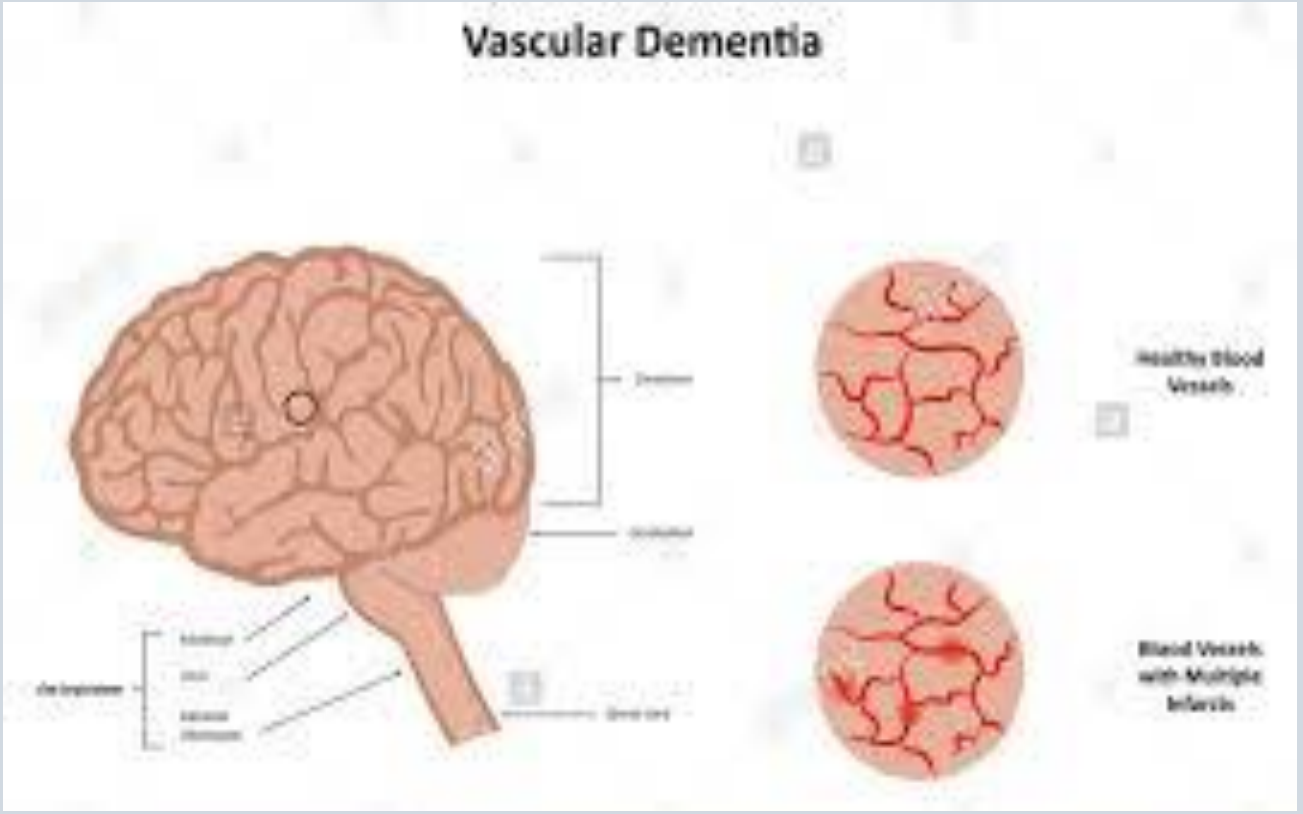
Mental Activity

Social Engagement

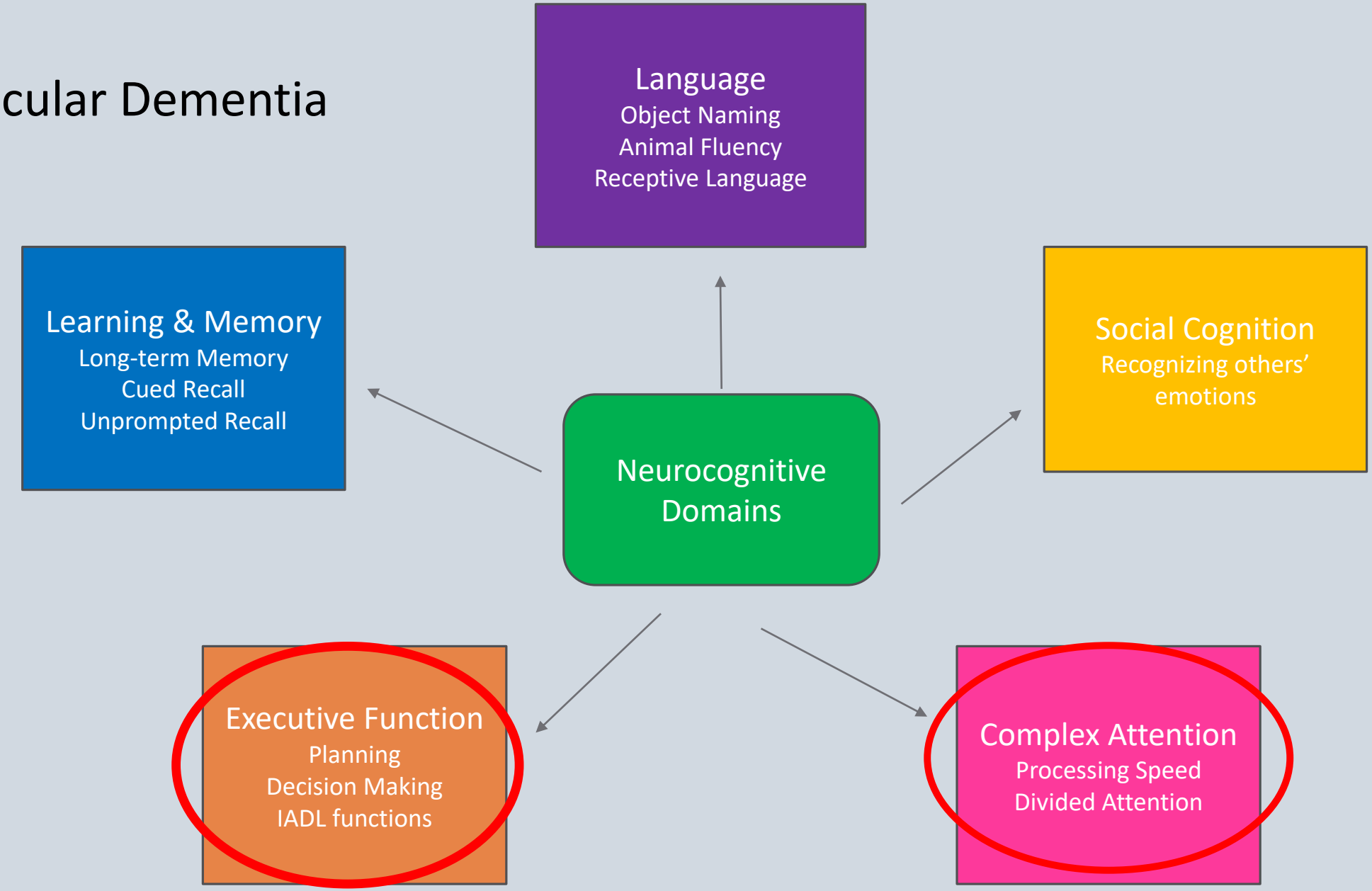
Music Therapy

Vascular Dementia





Vascular Dementia



Pathophysiology – Vascular Dementia

Uncontrolled Blood Pressure

Diabetes

High Cholesterol

Ischemic Stroke

Vascular Dementia - Treatments

Control Risk factors

- Diabetes
- Hypertension
- Hyperlipidemia
- Obstructed Sleep Apnea

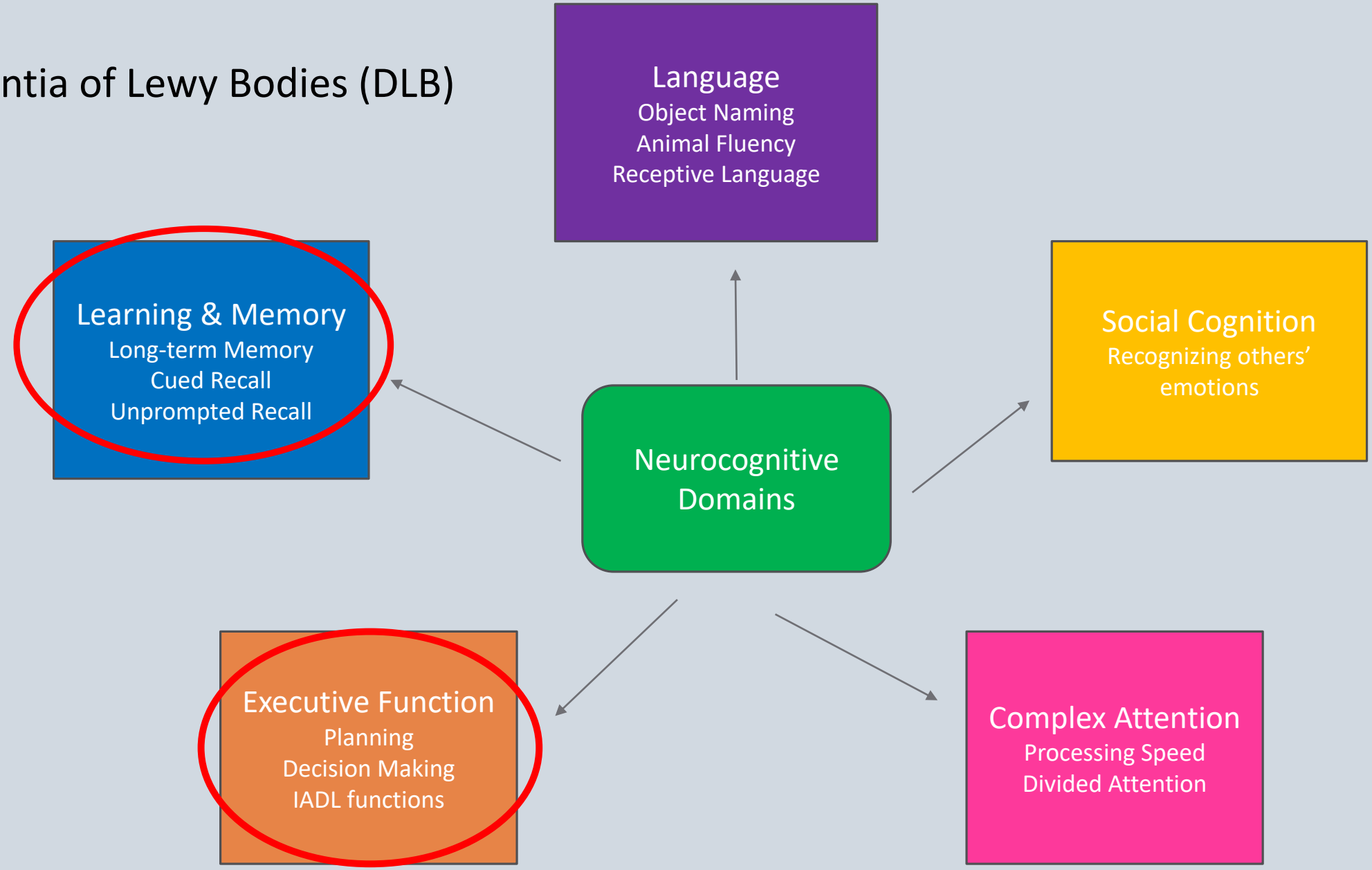
Acetylcholinesterase Inhibitors

- Donepezil (Aricept®)
- Galantamine (Reminyl®)
- Rivastigmine (Exelon®)

Memantine

- Limited evidence

Dementia of Lewy Bodies (DLB)



Lewy Body Dementia (DLB)

Presentation

- Fluctuating Cognition (“good and bad days”)
- Visual Hallucinations
- Parkinsonism Features

Pathology

- Lewy bodies located in cortex & midbrain

Dementia of Lewy Body - Treatments

Acetylcholinesterase Inhibitors

- 1st line treatment
- Donepezil (Aricept®)
- Galantamine (Reminyl®)
- Rivastigmine (Exelon®)

Memantine

- Mixed Results

Dementia of Lewy Body - Treatments

Antipsychotics

- Atypicals (olanzapine, quetiapine, pimavanserin, ziprasidone, aripiprazole, paliperidone)

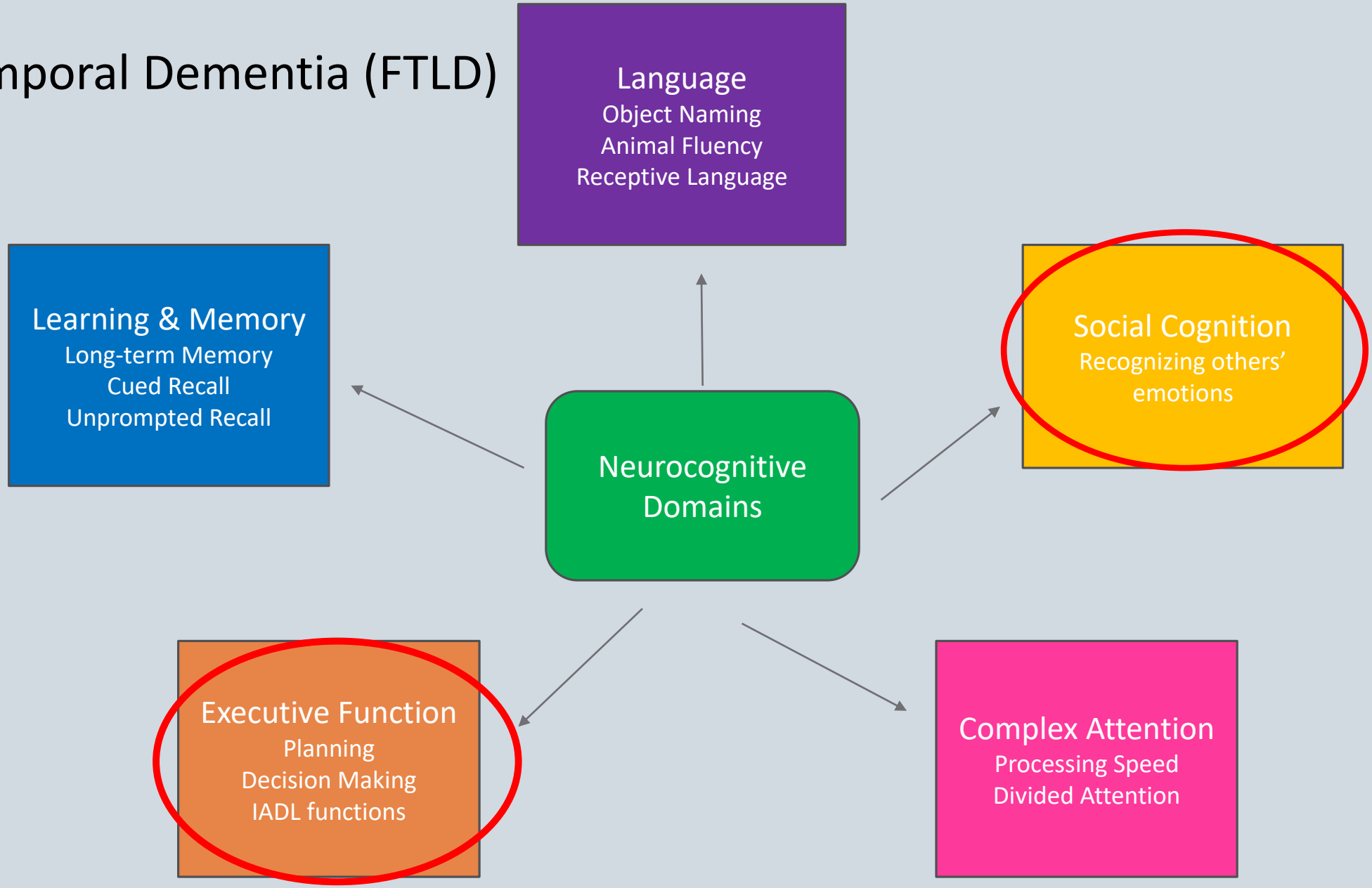
Parkinson Medications

- Levodopa

Orthostatic Hypotension

- Fludocortisone
- Midodrine

Frontotemporal Dementia (FTLD)



Frontotemporal Dementia (FTLD)

<65 years of age

Presentation:

- Behavioral Disinhibition
- Apathy or inertia
- Compulsive Behavior
- Preservative Behavior

Pathology:

- Absence of plagues & tangles

FTLD – Treatments

No FDA approved treatment

Nonpharmacological interventions

- Focus on safety and health maintenance

Acetylcholinesterase inhibitors

- Worsen symptoms

Prevention Strategies

Controlling Cardiovascular Risks

- Obesity, DM, HTN, HLD

Depression Management

Social Engagement

Early detection

AD Treatments: On the Horizon

Approved Symptomatic Treatments
- Donepezil (AChEI)
- Galantamine (AChEI)
- Rivastigmine (AChEI)
- Memantine (NMDA receptor antagonist)
- Donepezil + memantine combination (approved in the US)

Combination with disease-modifying therapies

Drug target	Agents
Amyloid cascade	• BACE inhibitors • Aβ monocolonal antibody • Aβ vaccine
Tau aggregates	• Tau active immunization • Tau passive immunization
Other	• Tyrosine kinase inhibitor • RAGE inhibitor • Anti-inflammatory • Angiotensin II receptor antagonist • Src/abl kinase family inhibitor • GM-CSF • Vitamin B3 • 11β–hydroxysteroid dehydrogenase inhibitor • Sigma-1 chaperone agonist • Deep brain stimulation • rTMS • Sigma-2 receptor ligand • PPARδ/γ agonist • Microtubule stabilizer

Combination with symptomatic therapies

Agents	Symptom target
• 5-HT receptor antagonist • MAO-B inhibitor • Anticonvulsant • Melatonin and serotonin receptor agonist • Glutamate neurotransmission modulator	Cognition, agitation, aggression, non convulsive seizures

Questions?

Email: lauren.welch@va.gov

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